



#14

SEQUENCE LISTING

<110> OXVIG, Claus
OVERGAARD, Michael T.

<120> PREGNANCY-ASSOCIATED PLASMA PROTEIN-A2 (PAPP-A2)

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<140> US 09/983,025
<141> 2001-10-22

<150> US 60/241,840
<151> 2000-10-20

<150> DK PA 2000 01571
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<170> PatentIn version 3.2

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Glu Pro Val Lys Val Gln Ser Ile Val Cys Thr Gly Arg Arg Gln	
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Trp His Pro Asp Pro Val Leu Val His Cys Ile Gln Ser Cys Glu	
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Tyr Cys His Tyr Asp Gly Gly Asp Cys Cys Ser Ser Thr Leu Ser	
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His Thr Gly Arg Ser Lys Pro Asp Thr Glu Gly Asn Ala Val Ser
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Lys Pro Glu Thr Gln Arg Arg Gly Trp Ala Lys Ser Arg Gln Arg Arg
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Gln Val Trp Lys Arg Arg Ala Glu Asp Gly Gln Gly Asp Ser Gly Ile
 -30 -25 -20

Ser Ser His Phe Gln Pro Trp Pro Lys His Ser Leu Lys His Arg Val
 -15 -10 -5

Lys Lys Ser Pro Pro Glu Glu Ser Asn Gln Asn Gly Gly Glu Gly Ser
 -1 1 5 10

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Tyr Phe Ser Gly Arg Arg Glu Arg Leu Leu Leu Arg Pro Glu Val Leu
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Ala Glu Ile Pro Arg Glu Ala Phe Thr Val Glu Ala Trp Val Lys Pro
 50 55 60

Glu Gly Gly Gln Asn Asn Pro Ala Ile Ile Ala Gly Val Phe Asp Asn
 65 70 75

Cys Ser His Thr Val Ser Asp Lys Gly Trp Ala Leu Gly Ile Arg Ser
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Gly Lys Asp Lys Gly Lys Arg Asp Ala Arg Phe Phe Phe Ser Leu Cys
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Thr Asp Arg Val Lys Lys Ala Thr Ile Leu Ile Ser His Ser Arg Tyr
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Gln Pro Gly Thr Trp Thr His Val Ala Ala Thr Tyr Asp Gly Arg His
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Met Ala Leu Tyr Val Asp Gly Thr Gln Val Ala Ser Ser Leu Asp Gln
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Ser Gly Pro Leu Asn Ser Pro Phe Met Ala Ser Cys Arg Ser Leu Leu
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Leu Gly Gly Asp Ser Ser Glu Asp Gly His Tyr Phe Arg Gly His Leu
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His Ser Ser Gln His Ser Ser Gly Glu Glu Glu Ala Thr Asp Leu Val
 210 215 220

Leu Thr Ala Ser Phe Glu Pro Val Asn Thr Glu Trp Val Pro Phe Arg
 225 230 235

Asp Glu Lys Tyr Pro Arg Leu Glu Val Leu Gln Gly Phe Glu Pro Glu
 240 245 250

Pro Glu Ile Leu Ser Pro Leu Gln Pro Pro Leu Cys Gly Gln Thr Val
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Cys Asp Asn Val Glu Leu Ile Ser Gln Tyr Asn Gly Tyr Trp Pro Leu
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Arg Gly Glu Lys Val Ile Arg Tyr Gln Val Val Asn Ile Cys Asp Asp
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Glu Gly Leu Asn Pro Ile Val Ser Glu Glu Gln Ile Arg Leu Gln His
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Glu Ala Leu Asn Glu Ala Phe Ser Arg Tyr Asn Ile Ser Trp Gln Leu
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Ser Val His Gln Val His Asn Ser Thr Leu Arg His Arg Val Val Leu
 335 340 345 350

Val Asn Cys Glu Pro Ser Lys Ile Gly Asn Asp His Cys Asp Pro Glu
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 370 375 380

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Thr	Asp	Thr	Met	Ile	His	Glu	Val	Gly	His	Val	Leu	Gly	Leu	Tyr	His	495	500	505	510
Val	Phe	Lys	Gly	Val	Ser	Glu	Arg	Glu	Ser	Cys	Asn	Asp	Pro	Cys	Lys	515	520	525	
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Pro	Thr	Pro	Lys	Ser	Glu	Leu	Cys	Arg	Glu	Pro	Glu	Pro	Thr	Ser	Asp	545	550	555	
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Gly	Thr	Phe	Arg	Gln	Tyr	Val	His	Thr	Ala	Ser	Ser	Arg	Arg	Val	Cys	655	660	665	670
Asp	Ser	Ser	Gly	Tyr	Trp	Thr	Pro	Glu	Glu	Ala	Val	Gly	Pro	Pro	Asp	675	680	685	
Val	Asp	Gln	Pro	Cys	Glu	Pro	Ser	Leu	Gln	Ala	Trp	Ser	Pro	Glu	Val	690	695	700	
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Lys Val Ser Gly Val Lys Val Tyr Thr Phe Asp Glu Arg Ile Glu Ile
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Asp Ala Ala Leu Leu Thr Ser Gln Pro His Ser Pro Leu Cys Ser Gly
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Cys Arg Pro Val Arg Tyr Gln Val Leu Arg Asp Pro Pro Phe Ala Ser
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Ala Pro Tyr Cys Gly Asp Gly Lys Val Ser Glu Arg Leu Gly Glu Glu
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Met Tyr Glu Gly Asp Gly Ile Cys Glu Pro Phe Glu Arg Lys Thr Ser
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Ile Val Asp Cys Gly Ile Tyr Thr Pro Lys Gly Tyr Leu Asp Gln Trp
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Cys Gly Lys Gln Asp Ser Cys Pro Ser Leu Leu Leu Asp His Ala
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Ser	Glu	Gly	Thr	Lys	Phe	Leu	Lys	Arg	Cys	Ser	Ile	Ser	Cys	Val
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Pro	Pro	Ala	Lys	Leu	Gln	Gly	Leu	Ser	Pro	Trp	Leu	Thr	Cys	Leu
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<223> synthetic myc epitope in pPA2-mH

<400> 19

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1 5 10

<210> 20
<211> 5
<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic linker in pPA2-mH

<400> 20

Asn Ser Ala Val Asp
1 5

<210> 21

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing XhoI site, for amplifying IGFBP-5 cDNA

<400> 21

tccgctcgag atggtgttgc tcaccgcggt

30

<210> 22

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> primer containing HindIII site, for amplifying IGFBP-5 cDNA

<400> 22

cgataagctt ctcaacgttg ctgctgtcg

29

<210> 23

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> N-terminal sequence of degradation product of purified rIGFBP-5
digested with PAPP-A2

<400> 23

Lys Phe Val Gly Gly Ala
1 5

<210> 24

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> N-terminal sequence of degradation product of purified rIGFBP-5
digested with PAPP-A2

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 <223> Xaa is unknown

<400> 24

Leu Gly Xaa Phe Val His
 1 5

<210> 25
 <211> 1627
 <212> PRT
 <213> Homo sapiens

<400> 25

Met Arg Leu Trp Ser Trp Val Leu His Leu Gly Leu Leu Ser Ala Ala
 1 5 10 15

Leu Gly Cys Gly Leu Ala Glu Arg Pro Arg Arg Ala Arg Arg Asp Pro
 20 25 30

Arg Ala Gly Arg Pro Pro Arg Pro Ala Ala Gly Pro Ala Thr Cys Ala
 35 40 45

Thr Arg Gly Pro Arg Pro Pro Arg Leu Ala Ala Ala Ala Ala Ala
 50 55 60

Gly Arg Ala Trp Glu Ala Val Arg Val Pro Arg Arg Arg Gln Gln Arg
 65 70 75 80

Glu Ala Arg Gly Ala Thr Glu Glu Pro Ser Pro Pro Ser Arg Ala Leu
 85 90 95

Tyr Phe Ser Gly Arg Gly Glu Gln Leu Arg Val Leu Arg Ala Asp Leu
 100 105 110

Glu Leu Pro Arg Asp Ala Phe Thr Leu Gln Val Trp Leu Arg Ala Glu
 115 120 125

Gly Gly Gln Arg Ser Pro Ala Val Ile Thr Gly Leu Tyr Asp Lys Cys
 130 135 140

Ser Tyr Ile Ser Arg Asp Arg Gly Trp Val Val Gly Ile His Thr Ile
 145 150 155 160

Ser Asp Gln Asp Asn Lys Asp Pro Arg Tyr Phe Phe Ser Leu Lys Thr
 165 170 175

Asp Arg Ala Arg Gln Val Thr Thr Ile Asn Ala His Arg Ser Tyr Leu
 180 185 190

Pro Gly Gln Trp Val Tyr Leu Ala Ala Thr Tyr Asp Gly Gln Phe Met
 195 200 205

Lys Leu Tyr Val Asn Gly Ala Gln Val Ala Thr Ser Gly Glu Gln Val
 210 215 220

Gly Gly Ile Phe Ser Pro Leu Thr Gln Lys Cys Lys Val Leu Met Leu
 225 230 235 240

Gly Gly Ser Ala Leu Asn His Asn Tyr Arg Gly Tyr Ile Glu His Phe
 245 250 255

Ser Leu Trp Lys Val Ala Arg Thr Gln Arg Glu Ile Leu Ser Asp Met
 260 265 270

Glu Thr His Gly Ala His Thr Ala Leu Pro Gln Leu Leu Leu Gln Glu
 275 280 285

Asn Trp Asp Asn Val Lys His Ala Trp Ser Pro Met Lys Asp Gly Ser
 290 295 300

Ser Pro Lys Val Glu Phe Ser Asn Ala His Gly Phe Leu Leu Asp Thr
 305 310 315 320

Ser Leu Glu Pro Pro Leu Cys Gly Gln Thr Leu Cys Asp Asn Thr Glu
 325 330 335

Val Ile Ala Ser Tyr Asn Gln Leu Ser Ser Phe Arg Gln Pro Lys Val
 340 345 350

Val Arg Tyr Arg Val Val Asn Leu Tyr Glu Asp Asp His Lys Asn Pro
 355 360 365

Thr Val Thr Arg Glu Gln Val Asp Phe Gln His His Gln Leu Ala Glu
 370 375 380

Ala Phe Lys Gln Tyr Asn Ile Ser Trp Glu Leu Asp Val Leu Glu Val
385 390 395 400

Ser Asn Ser Ser Leu Arg Arg Arg Leu Ile Leu Ala Asn Cys Asp Ile
405 410 415

Ser Lys Ile Gly Asp Glu Asn Cys Asp Pro Glu Cys Asn His Thr Leu
420 425 430

Thr Gly His Asp Gly Gly Asp Cys Arg His Leu Arg His Pro Ala Phe
435 440 445

Val Lys Lys Gln His Asn Gly Val Cys Asp Met Asp Cys Asn Tyr Glu
450 455 460

Arg Phe Asn Phe Asp Gly Gly Glu Cys Cys Asp Pro Glu Ile Thr Asn
465 470 475 480

Val Thr Gln Thr Cys Phe Asp Pro Asp Ser Pro His Arg Ala Tyr Leu
485 490 495

Asp Val Asn Glu Leu Lys Asn Ile Leu Lys Leu Asp Gly Ser Thr His
500 505 510

Leu Asn Ile Phe Phe Ala Lys Ser Ser Glu Glu Glu Leu Ala Gly Val
515 520 525

Ala Thr Trp Pro Trp Asp Lys Glu Ala Leu Met His Leu Gly Gly Ile
530 535 540

Val Leu Asn Pro Ser Phe Tyr Gly Met Pro Gly His Thr His Thr Met
545 550 555 560

Ile His Glu Ile Gly His Ser Leu Gly Leu Tyr His Val Phe Arg Gly
565 570 575

Ile Ser Glu Ile Gln Ser Cys Ser Asp Pro Cys Met Glu Thr Glu Pro
580 585 590

Ser Phe Glu Thr Gly Asp Leu Cys Asn Asp Thr Asn Pro Ala Pro Lys
595 600 605

His Lys Ser Cys Gly Asp Pro Gly Pro Gly Asn Asp Thr Cys Gly Phe
610 615 620

His	Ser	Phe	Phe	Asn	Thr	Pro	Tyr	Asn	Asn	Phe	Met	Ser	Tyr	Ala	Asp	625	630	635	640
Asp	Asp	Cys	Thr	Asp	Ser	Phe	Thr	Pro	Asn	Gln	Val	Ala	Arg	Met	His	645	650	655	
Cys	Tyr	Leu	Asp	Leu	Val	Tyr	Gln	Gly	Trp	Gln	Pro	Ser	Arg	Lys	Pro	660	665	670	
Ala	Pro	Val	Ala	Leu	Ala	Pro	Gln	Val	Leu	Gly	His	Thr	Thr	Asp	Ser	675	680	685	
Val	Thr	Leu	Glu	Trp	Phe	Pro	Pro	Ile	Asp	Gly	His	Phe	Phe	Glu	Arg	690	695	700	
Glu	Leu	Gly	Ser	Ala	Cys	His	Leu	Cys	Leu	Glu	Gly	Arg	Ile	Leu	Val	705	710	715	720
Gln	Tyr	Ala	Ser	Asn	Ala	Ser	Ser	Pro	Met	Pro	Cys	Ser	Pro	Ser	Gly	725	730	735	
His	Trp	Ser	Pro	Arg	Glu	Ala	Glu	Gly	His	Pro	Asp	Val	Glu	Gln	Pro	740	745	750	
Cys	Lys	Ser	Ser	Val	Arg	Thr	Trp	Ser	Pro	Asn	Ser	Ala	Val	Asn	Pro	755	760	765	
His	Thr	Val	Pro	Pro	Ala	Cys	Pro	Glu	Pro	Gln	Gly	Cys	Tyr	Leu	Glu	770	775	780	
Leu	Glu	Phe	Leu	Tyr	Pro	Leu	Val	Pro	Glu	Ser	Leu	Thr	Ile	Trp	Val	785	790	795	800
Thr	Phe	Val	Ser	Thr	Asp	Trp	Asp	Ser	Ser	Gly	Ala	Val	Asn	Asp	Ile	805	810	815	
Lys	Leu	Leu	Ala	Val	Ser	Gly	Lys	Asn	Ile	Ser	Leu	Gly	Pro	Gln	Asn	820	825	830	
Val	Phe	Cys	Asp	Val	Pro	Leu	Thr	Ile	Arg	Leu	Trp	Asp	Val	Gly	Glu	835	840	845	

Glu Val Tyr Gly Ile Gln Ile Tyr Thr Leu Asp Glu His Leu Glu Ile
850 855 860

Asp Ala Ala Met Leu Thr Ser Thr Ala Asp Thr Pro Leu Cys Leu Gln
865 870 875 880

Cys Lys Pro Leu Lys Tyr Lys Val Val Arg Asp Pro Pro Leu Gln Met
885 890 895

Asp Val Ala Ser Ile Leu His Leu Asn Arg Lys Phe Val Asp Met Asp
900 905 910

Leu Asn Leu Gly Ser Val Tyr Gln Tyr Trp Val Ile Thr Ile Ser Gly
915 920 925

Thr Glu Glu Ser Glu Pro Ser Pro Ala Val Thr Tyr Ile His Gly Arg
930 935 940

Gly Tyr Cys Gly Asp Gly Ile Ile Gln Lys Asp Gln Gly Glu Gln Cys
945 950 955 960

Asp Asp Met Asn Lys Ile Asn Gly Asp Gly Cys Ser Leu Phe Cys Arg
965 970 975

Gln Glu Val Ser Phe Asn Cys Ile Asp Glu Pro Ser Arg Cys Tyr Phe
980 985 990

His Asp Gly Asp Gly Val Cys Glu Glu Phe Glu Gln Lys Thr Ser Ile
995 1000 1005

Lys Asp Cys Gly Val Tyr Thr Pro Gln Gly Phe Leu Asp Gln Trp
1010 1015 1020

Ala Ser Asn Ala Ser Val Ser His Gln Asp Gln Gln Cys Pro Gly
1025 1030 1035

Trp Val Ile Ile Gly Gln Pro Ala Ala Ser Gln Val Cys Arg Thr
1040 1045 1050

Lys Val Ile Asp Leu Ser Glu Gly Ile Ser Gln His Ala Trp Tyr
1055 1060 1065

Pro Cys Thr Ile Ser Tyr Pro Tyr Ser Gln Leu Ala Gln Thr Thr
1070 1075 1080

Phe	Trp	Leu	Arg	Ala	Tyr	Phe	Ser	Gln	Pro	Met	Val	Ala	Ala	Ala
1085						1090					1095			
Val	Ile	Val	His	Leu	Val	Thr	Asp	Gly	Thr	Tyr	Tyr	Gly	Asp	Gln
1100						1105					1110			
Lys	Gln	Glu	Thr	Ile	Ser	Val	Gln	Leu	Leu	Asp	Thr	Lys	Asp	Gln
1115						1120					1125			
Ser	His	Asp	Leu	Gly	Leu	His	Val	Leu	Ser	Cys	Arg	Asn	Asn	Pro
1130						1135					1140			
Leu	Ile	Ile	Pro	Val	Val	His	Asp	Leu	Ser	Gln	Pro	Phe	Tyr	His
1145						1150					1155			
Ser	Gln	Ala	Val	Arg	Val	Ser	Phe	Ser	Ser	Pro	Leu	Val	Ala	Ile
1160						1165					1170			
Ser	Gly	Val	Ala	Leu	Arg	Ser	Phe	Asp	Asn	Phe	Asp	Pro	Val	Thr
1175						1180					1185			
Leu	Ser	Ser	Cys	Gln	Arg	Gly	Glu	Thr	Tyr	Ser	Pro	Ala	Glu	Gln
1190						1195					1200			
Ser	Cys	Val	His	Phe	Ala	Cys	Glu	Lys	Thr	Asp	Cys	Pro	Glu	Leu
1205						1210					1215			
Ala	Val	Glu	Asn	Ala	Ser	Leu	Asn	Cys	Ser	Ser	Ser	Asp	Arg	Tyr
1220						1225					1230			
His	Gly	Ala	Gln	Cys	Thr	Val	Ser	Cys	Arg	Thr	Gly	Tyr	Val	Leu
1235						1240					1245			
Gln	Ile	Arg	Arg	Asp	Asp	Glu	Leu	Ile	Lys	Ser	Gln	Thr	Gly	Pro
1250						1255					1260			
Ser	Val	Thr	Val	Thr	Cys	Thr	Glu	Gly	Lys	Trp	Asn	Lys	Gln	Val
1265						1270					1275			
Ala	Cys	Glu	Pro	Val	Asp	Cys	Ser	Ile	Pro	Asp	His	His	Gln	Val
1280						1285					1290			

Tyr	Ala	Ala	Ser	Phe	Ser	Cys	Pro	Glu	Gly	Thr	Thr	Phe	Gly	Ser
1295						1300					1305			
Gln	Cys	Ser	Phe	Gln	Cys	Arg	His	Pro	Ala	Gln	Leu	Lys	Gly	Asn
1310						1315					1320			
Asn	Ser	Leu	Leu	Thr	Cys	Met	Glu	Asp	Gly	Leu	Trp	Ser	Phe	Pro
1325						1330					1335			
Glu	Ala	Leu	Cys	Glu	Leu	Met	Cys	Leu	Ala	Pro	Pro	Pro	Val	Pro
1340						1345					1350			
Asn	Ala	Asp	Leu	Gln	Thr	Ala	Arg	Cys	Arg	Glu	Asn	Lys	His	Lys
1355						1360					1365			
Val	Gly	Ser	Phe	Cys	Lys	Tyr	Lys	Cys	Lys	Pro	Gly	Tyr	His	Val
1370						1375					1380			
Pro	Gly	Ser	Ser	Arg	Lys	Ser	Lys	Lys	Arg	Ala	Phe	Lys	Thr	Gln
1385						1390					1395			
Cys	Thr	Gln	Asp	Gly	Ser	Trp	Gln	Glu	Gly	Ala	Cys	Val	Pro	Val
1400						1405					1410			
Thr	Cys	Asp	Pro	Pro	Pro	Pro	Lys	Phe	His	Gly	Leu	Tyr	Gln	Cys
1415						1420					1425			
Thr	Asn	Gly	Phe	Gln	Phe	Asn	Ser	Glu	Cys	Arg	Ile	Lys	Cys	Glu
1430						1435					1440			
Asp	Ser	Asp	Ala	Ser	Gln	Gly	Leu	Gly	Ser	Asn	Val	Ile	His	Cys
1445						1450					1455			
Arg	Lys	Asp	Gly	Thr	Trp	Asn	Gly	Ser	Phe	His	Val	Cys	Gln	Glu
1460						1465					1470			
Met	Gln	Gly	Gln	Cys	Ser	Val	Pro	Asn	Glu	Leu	Asn	Ser	Asn	Leu
1475						1480					1485			
Lys	Leu	Gln	Cys	Pro	Asp	Gly	Tyr	Ala	Ile	Gly	Ser	Glu	Cys	Ala
1490						1495					1500			
Thr	Ser	Cys	Leu	Asp	His	Asn	Ser	Glu	Ser	Ile	Ile	Leu	Pro	Met
1505						1510					1515			

Asn Val Thr Val Arg Asp Ile Pro His Trp Leu Asn Pro Thr Arg
 1520 1525 1530

 Val Glu Arg Val Val Cys Thr Ala Gly Leu Lys Trp Tyr Pro His
 1535 1540 1545

 Pro Ala Leu Ile His Cys Val Lys Gly Cys Glu Pro Phe Met Gly
 1550 1555 1560

 Asp Asn Tyr Cys Asp Ala Ile Asn Asn Arg Ala Phe Cys Asn Tyr
 1565 1570 1575

 Asp Gly Gly Asp Cys Cys Thr Ser Thr Val Lys Thr Lys Lys Val
 1580 1585 1590

 Thr Pro Phe Pro Met Ser Cys Asp Leu Gln Gly Asp Cys Ala Cys
 1595 1600 1605

 Arg Asp Pro Gln Ala Gln Glu His Ser Arg Lys Asp Leu Arg Gly
 1610 1615 1620

 Tyr Ser His Gly
 1625

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 <213> Artificial

<220>
 <223> An elongated zinc binding motif

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 <222> (3)..(4)
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 <222> (6)..(7)
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<220>
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 <222> (9)..(10)
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C2
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